REVIEW

A quantitative estimate of bare-metal stenting compared with balloon angioplasty in patients with acute myocardial infarction: angiographic measures in relation to clinical outcome

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We performed a systematic review of all randomised controlled trials (RCTs) from the pre-drug-eluting-stent era comparing bare-metal stenting (BMS) with balloon angioplasty in patients with acute myocardial infarction (MI) to examine coronary angiographic parameters of infarct-related vessel patency and to relate the angiographic measures to clinical outcome. The search was restricted to published RCTs in humans. 10 RCTs, (6192 patients) were analysed. Compared with balloon angioplasty, BMS was associated with reduced rates of reocclusion (6.7% vs 10.1%, OR 0.62, 95% CI 0.40 to 0.96, p = 0.03) and restenosis (23.9% vs 39.3%, OR 0.45, 95% CI 0.34 to 0.59, p<0.001), but not with reduced rates of subacute thrombosis (1.7% in both groups). BMS showed a reduction in target vessel revascularisation (TVR; 12.2% vs 19.2%, OR 0.50, 95% CI 0.37 to 0.69, p<0.001), but not in mortality (5.3% vs 5.1%) or reinfarction (3.9% vs 4%). The findings of this study support BMS placement in acute MI. The discrepancy between angiographic and clinical parameters has important implications for future studies investigating further technical improvements in mechanical reperfusion therapy.

Primary percutaneous coronary intervention (PCI) has emerged as the preferred treatment of acute myocardial infarction (MI) and has been proven to be a very effective method to obtain patency of the infarct-related vessel.[1–3] Although the outcome of patients with acute MI has clearly improved with primary PCI, abrupt vessel closure in the hours to days after the PCI procedure, as well as restenosis and reocclusion in the months after the procedure, are still limitations of this treatment modality. To address these limitations, intracoronary bare-metal stent (BMS) placement in addition to balloon angioplasty has been introduced. During the past decade, BMS implantation during PCI in the treatment of acute MI has become a common practice, and is included as a class Ia recommendation in the guidelines for PCIs of the European Society of Cardiology.[3] The potential benefits of BMS compared with balloon angioplasty during PCI in acute MI have been studied in several trials[4–16] and meta-analyses of randomised controlled trials (RCTs).[17–21] These studies have been focusing on clinical end points and in general have shown that routine use of BMS reduces the need for revascularisation of the infarct-related vessel, but does not convincingly improve 1-year survival or lower the risk of reinfarction. With the introduction and ongoing investigation of the benefit of drug-eluting stents during PCI, it is unlikely that prospective studies to address the question of mortality and reinfarction after BMS placement compared with balloon angioplasty will be performed, and current practice is mainly based on a beneficial effect of BMS on subsequent revascularisation rates as a measure of infarct-related vessel patency. Previous analyses have been inconclusive on angiographic measures of infarct-related vessel patency, in particular on rates of reocclusion and subacute thrombosis. The ischaemia-driven revascularisations used in most of the analysed trials do not necessarily reflect the real rates of reocclusion and restenosis as these events may occur silently—that is, without ischaemic symptoms.[22] The parameters of infarct-related vessel patency are of importance because reocclusion of the infarct-related vessel in the first months after the PCI procedure has been shown to be a predictor of reduced left ventricular function and cardiovascular mortality in up to 8 years of follow-up.[23–27] We believe that an analysis of angiographic parameters of infarct-related vessel patency will give more evidence to the use of BMS in primary PCI. Also, we consider an overview of these parameters important for future trials investigating further improvements in mechanical reperfusion therapy.

We performed a systematic review to quantify the treatment effect of BMS in primary PCI on angiographic measures of infarct-related artery patency in relation to clinical outcomes. We analysed all RCTs comparing BMS implantation to balloon angioplasty in the treatment of patients with acute MI.

METHODS

Study identification

We sought to identify all relevant published randomised trials comparing BMS with balloon

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Abbreviations: BMS, bare-metal stent; CABG, coronary artery bypass grafting; MI, myocardial infarction; PCI, percutaneous coronary intervention; PAMI, Primary Angioplasty in Myocardial Infraction; RCT, randomised controlled trial; TIMI, thrombolysis in myocardial infarction; TVR, target vessel revascularisation

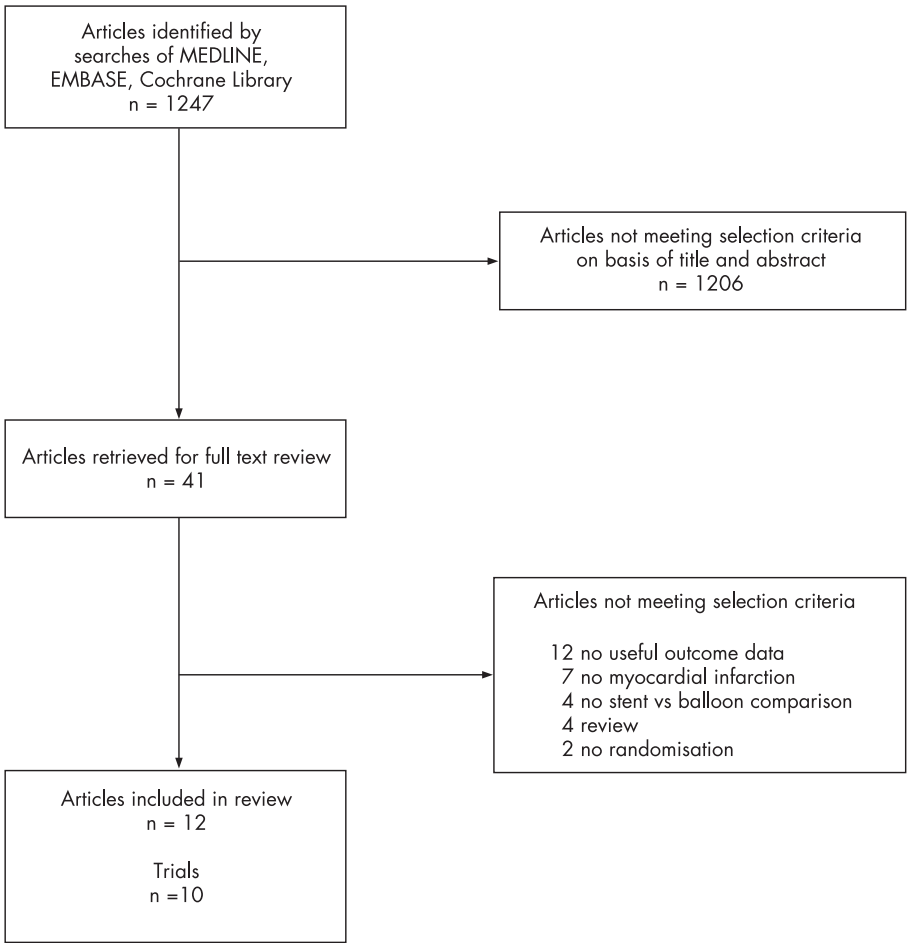

Figure 1 Flow diagram trial selection.

angioplasty in the treatment of patients with acute MI. A literature search of MEDLINE and EMBASE from 1990 to February 2006 and the Cochrane Library (2005, Issue 2) was performed. Search terms included a combination of index terms (myocardial infarction/therapy; myocardial revascularisation; stents; angioplasty; percutaneous transluminal coronary; balloon dilatation) and free text words or word stems (myocardial infarct*; stent*; balloon; dilatat*; angioplasty). The search was restricted to studies conducted in humans and classified as RCTs. No language restriction was used. In addition, we examined relevant reviews and reference lists of retrieved studies.

Study selection

Two investigators (IvdH and TS) independently evaluated studies for eligibility. Criteria for inclusion were: (1) randomised treatment allocation; (2) inclusion of patients with objectively diagnosed acute MI; (3) comparison of primary BMS with primary balloon angioplasty; and (4) available core-laboratory

Table 1 Description of trials

Trial	Year	Sites, n	Patients, n	Patients BMS, n	Patients B, n	Time from SO, h	Vessel size, mm	Crossover BMS, n (%)	Cross-over B, n (%)	Clinical follow-up, months	Angiographic follow-up, months
FRESCO[5]	1998	1	150	75	75	<6 (6–24*)	>2.5	0 (0)	0 (0)	6	6
GRAMI[6]	1998	8	104	52	52	<24	>2.5	0 (0)	13 (25)	12	0.24
ZWOLLE I[7]	1998	1	227	112	115	<6 (6–24*)	>3.0	2 (2)	15 (13)	24	6
Stent PAMI[8]	1999	62	900	452	448	<12	3.0–4.5	7 (2)	67 (15)	12	6
PASTA[9]	1999	6	136	67	69	<12	>2.5	1 (1)	7 (10)	12	6
STENTIM-2[10]	2000	17	211	101	110	<12	>3.0	3 (3)	33 (36)	12	6
Psaami[11]	2001	1	88	44	44	<6 (6–24*)	>3.0	1(2)	12 (27)	24	6
CADILLAC[12]	2002	76	2082	1036	1046	<12	2.5–4.5	22 (1)	168 (18)	6	7
STOPAMI 3[13]	2004	611	611	305	306	<48	All	14 (5)	93 (30)	6	NA
ZWOLLE II[14]	2005	1	1683	849	834	<6 (6–24*)	All	109 (13)	214 (26)	12	6
Total			6192	3093	3099			159 (5.1)	622 (20.1)		

B, balloon group; BMS, bare-metal stent group; SO, symptom onset; NA, not available.
*For continuing myocardial ischaemia; NA
Year, year of publication; Sites, number of centres involved in trial

Table 2 Procedural data

Trial	PCI performed		MVD		PreTIMI 0/1		PostTIMI 3		CABG		Bleeding	
	BMS, n	B, n	BMS, n (%)	B n (%)	BMS n (%)	B n (%)	BMS	B n (%)	BMS n (%)	B n (%)	BMS n (%)	B n (%)
FRESCO[5]	75	75	34	33	NA	NA	74	75	NA	NA	3	3
GRAMI[6]	52	52	NA	NA	41	42	50	43	0	1	1	1
ZWOLLE I[7]	112	115	49	51	NA	NA	110	110	2	1	7	3
Stent PAMI[8]	452	448	208	297	NA	NA	404	415	1	1	23	17
PASTA[9]	67	69	25	31	62	65	66	67	NA	NA	1	1
STENTIM-2[10]	101	110	31	36	101	110	85	75	NA	NA	NA	NA
Psaami[11]	44	44	10*	10*	44†	44†	41	39	NA	NA	4	6
CADILLAC[12]	1036	1046	514	502	694	720	992	998	NA	NA	5	5
STOPAMI-3[13]	305	306	205	200	192	208	295	292	8	11	4	6
Zwolle II[14]	785	763	458	453	558	576	745	732	27	25	NA	NA
Total	3029	3028	1534 (52)	1513 (51)	1692 (71)	1765 (74)	2862 (94)	2846 (93)	38 (2)‡	39 (2)‡	48 (2)‡	42 (2)‡

B, balloon group; BMS, bare-metal stent group; CABG, coronary artery bypass graft; MVD, multivessel disease (>1 coronary vessel diseased); PCI, percutaneous coronary intervention; PAMI, Primary Angioplasty in Myocardial Infraction; TIMI, thrombolysis in myocardial infarction; pre-TIMI 0/1, pre-procedural TIMI grade 0/1; post-TIMI 3, post-procedural TIMI grade 3; NA, not available.
*Three-vessel disease.
†TIMI 0/1/2.
‡Number of PCI performed based on studies with available data.

data on quantitative angiographic analysis and clinical outcomes at follow-up. Exclusion criteria were: (1) rescue angioplasty; (2) intervention >48 h after onset of symptoms; (3) exclusive inclusion of patients with cardiogenic shock; (4) coronary artery bypass grafts/small vessels; (5) use of drug-eluting stents or thrombectomy device; (6) no useful outcome data; and (7) reviews. Any disagreements were resolved by consensus.

Data abstraction and validity assessment

All data were abstracted independently by two investigators (FZ and TS) in duplicate using a prespecified reporting form. We extracted information on trial characteristics, including randomisation sequence, and outcome parameters (see below). Only outcome measures reported on an intention-to-treat basis were used in the analysis. Authors were contacted for additional and missing information. Discrepancies were resolved by consensus.

We chose not to use quality scoring that weighed the contribution of each study to the meta-analysis. The main criticism of incorporating quality scoring weights into meta-analyses is that there are no validated measures of quality and the use of subjective rating scales may lead to bias.[28] We considered the use of core-laboratory analysis of such importance for the quality of the study that we decided to make this a separate inclusion criterion. Angiographic follow-up results of <6 months after the acute event were not included in the pooled analysis. Descriptive follow-up data of <6 months were included with a remark.

Outcomes, definitions and data analysis

Primary angiographic outcomes of interest were the rates of reocclusion, restenosis and subacute thrombosis at angiographic follow-up. The examined secondary angiographic outcomes included thrombolysis in myocardial infarction (TIMI) flow 3 after coronary intervention as a measure of successful infarct-related artery reperfusion, and quantitative coronary angiographic parameters after coronary intervention and at follow-up. In addition, we examined crossover rates in both groups. We used the definition of restenosis as a stenosis of >50% and reocclusion as a totally occluded lesion. For subacute thrombosis, we have made use of the data reported in the trials. If rates of subacute thrombosis were not given, but if information was available on patients with angiographically documented reocclusion and reinfarction in the 30-day follow-up period, we included this as subacute thrombosis.

The clinical outcomes at the longest available follow-up investigated were rates of: all-cause mortality, myocardial reinfarction, target vessel revascularisation, emergency coronary artery bypass grafting (CABG) and bleeding complications. Myocardial reinfarction was defined as recurrent chest pain with new ST segment elevation and recurrent increase of cardiac enzymes. Target vessel revascularisation (TVR) was defined as percutaneous or surgical revascularisation of the infarct-related artery. For bleeding complications, we included bleeding requiring transfusion or surgical repair and intracerebral haemorrhage.

Data from all studies reporting on identical end points were pooled using Review Manager (RevMan) V.4.2 for Windows of the Cochrane Collaboration (www.cochrane.org). Dichotomous variables are reported as proportions and percentages, and continuous variables as mean values. Binary outcomes from individual studies were to be combined with both the Mantel Haenzel fixed effect model[29] and the random effects model.[30 31] The odds ratio (OR) and 95% CI were used as summary statistics for the comparison of dichotomous variables between BMS and balloon angioplasty. Reported values were two tailed, and results were considered statistically significant at $p<0.05$. For testing heterogeneity, statistical significance was accepted at a probability value of 0.10. This study was performed in

Table 3 Angiographic data after intervention and at follow-up

	Post-procedure						Follow-up							
	RD		MLD		DS		Patients		RD		MLD		DS	
Trial	BMS, mm	B, mm	BMS, mm	B, mm	BMS, mm	B, mm	BMS, mm	B, mm	BMS, mm	B, mm	BMS, mm	B, mm	BMS, mm	B, mm
FRESCO[5]	NA	NA	3.3	3.0	−4.0	5.0	68	56	NA	NA	2.4	2.0	NA	NA
GRAMI[6]*	3.0	3.1	2.7	2.3	10.0	27.6	50	50	3.0	3.1	2.7	2.0	10.8	36.2
ZWOLLE I[7]	3.2	3.1	2.6	2.2	17.9	28.8	101	96	3.1	3.1	2.0	1.6	33.4	47.3
Stent PAMI[8]	2.9	2.8	2.6	2.1	11.1	25.1	348	348	2.8	2.9	1.8	1.6	35.6	44.7
PASTA[9]	3.1	3.1	2.9	2.5	9.8	18.9	64	64	3.1	3.0	2.2	1.7	26.8	42.8
STENTIM-2[10]	3.0	3.0	2.4	2.1	19.4	28.5	101	110	2.9	2.8	1.7	1.5	42.5	46.8
PSAAMI[11]	NA	NA	3.1	2.6	NA	NA	37	33	NA	NA	2.2	1.5	NA	NA
CADILLAC[12]	3.0	3.0	2.7	2.2	11.0	25.0	325	311	3.0	3.0	2.7	2.2	11.0	25.0
STOPAMI 3[13]†	2.9	2.9	2.8	2.3	NA	NA.	305	306	NA	NA	NA	NA	NA	NA
ZWOLLE II[14]†	3.1	3.0	2.5	2.2	17.6	27.3	306	323	3.1	3.0	1.6	1.5	44.5	48.3

RD, reference diameter; MLD, minimal lumen diameter; DS, diameter stenosis; BMS, bare-metal stent group; B, balloon group; NA, not available; PAMI, Primary Angioplasty in Myocardial Infarction
*Follow-up 7 d.
†Follow-up 1 month.
‡RD post-procedure and follow-up.

compliance with the Quality of Reporting of Meta-Analyses guidelines.[32]

RESULTS

Study selection and trial characteristics

A flow diagram of the literature search is shown in fig 1. Our search yielded 12 studies out of 10 trials: FRESCO,[5] GRAMI,[6] ZWOLLE I,[7 15] Stent PAMI,[8 16] PASTA,[9] STENTIM-2,[10] PSAAMI,[11] CADILLAC,[12] STOPAMI-3[13] and ZWOLLE II.[14] Two trials (ZWOLLE I and Stent-PAMI) were referred to by two citations of which both provided useful information on outcomes and follow-up results. Three trials were excluded because the information had only been presented as an abstract and the reported data were insufficient for our analysis. These were among the articles that did not meet the selection criteria after retrieval of more information (fig 1).

The 10 included trials were published between 1998 and 2005 and involved 6192 patients, of which 3093 had been randomised to the BMS group and 3099 to the balloon group. Table 1 shows the characteristics of the trials. In general, the included lesions in the trials were in medium-calibre vessels. Crossover rates to BMS implantation in the balloon groups varied from 0 to 36%, and cross-over rates to balloon angioplasty in the BMS groups varied from 0% to 13%.

Depending on the study design, the use of concomitant pharmacotherapy varied somewhat between the trials with respect to antiplatelet treatment and use of abciximab. In most trials, antiplatelet treatment with ticlodipine was administered for 4 weeks after PCI in the BMS group. In two of the earlier trials, the duration of administration was 2 months (both BMS and balloon groups)[5] and 4 months.[8] In one of the early trials,[7] anticoagulation with coumadines was used in some patients receiving a BMS instead of dual antiplatelet treatment. In most trials, abciximab was used in <5% of the patients, in two trials abciximab was used in half of the patients,[11 12] and in one trial Abciximab was used in most patients (90%).[13]

The number of patients undergoing repeat angiography was specified in all trials, with the exception of two trials.[10 13] The rates of repeat angiography were roughly the same in both treatment groups of each of the trials. In two trials, the time of angiographic follow-up was 7 days[6] and 1 month[13] and the pooled angiographic data regarding restenosis and reocclusion rates of these trials were not included in the analysis. In all other trials, angiographic follow-up was performed at approximately 6 months (table 1).

We measured significant statistical heterogeneity between trials in the assessment of postprocedural TIMI flow 3 ($p = 0.03$), restenosis ($p = 0.05$), reinfarction ($p = 0.09$), and TVR ($p<0.001$), and we chose to present the results by the random effects model.

OUTCOME

Procedural and angiographic data

Table 2 summarises the procedural and angiographic data. There were no differences between the BMS and the balloon

Table 4 Angiographic data at follow-up

	Patients		RO		RS		SAT	
Trial	BMS, n	B, n	BMS, n (%)	B, n (%)	BMS, n (%)	B, n (%)	BMS, n (%)	B, n (%)
FRESCO[5]	68	56	NA	NA	NA	NA	NA	NA
ZWOLLE I[7]	101	96	4	6	12	33	1	5
Stent PAMI[8]	348	348	18	32	71	117	4	5
PASTA[9]	64	64	2	10	11	24	2	3
STENTIM-2[10]	101	110	7	6	26	44	NA	NA
PSAAMI[11]	37	33	1	4	9	20	NA	NA
CADILLAC[12]	325	311	19	37	72	130	5	14
STOPAMI 3[13]	305	306	NA	NA	NA	NA	6	4
ZWOLLE II[14]	306	323	35	35	105	137	29	18
Total			86/1282 (6.7)	134/1285 (10.1)	306/1282 (23.9)	505/1285 (39.3)	47/2821 (1.7)	49/2818 (1.7)

BMS, bare-metal stent group; B, balloon group; NA, not available; PAMI, Primary Angioplasty in Myocardial Infraction; RS, restenosis; RO, reocclusion; SAT, subacute thrombosis.

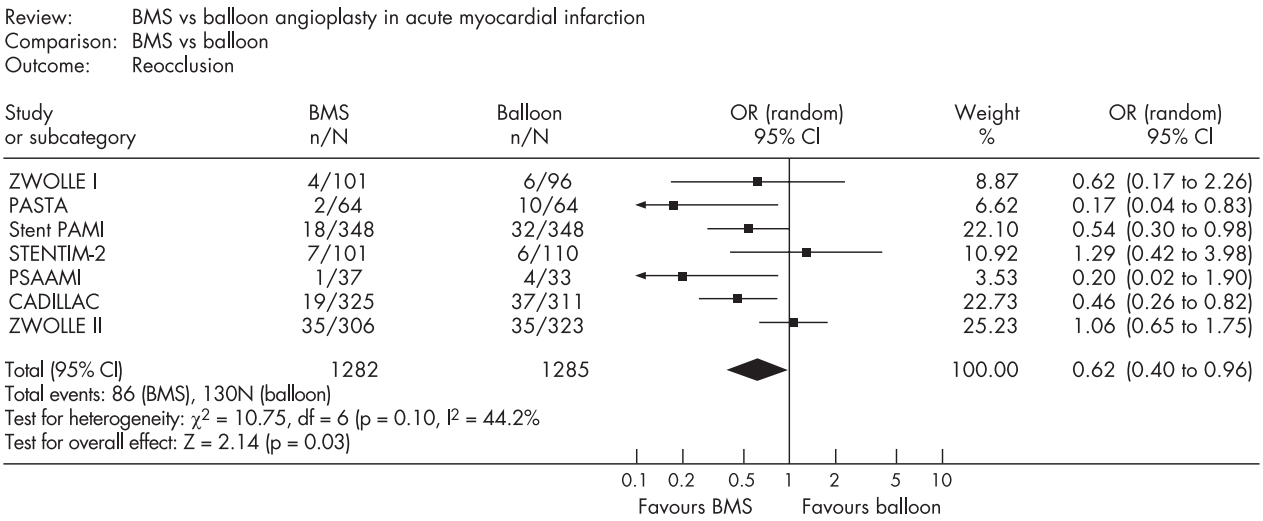

Figure 2 Reocclusion. BMS, bare-metal stent.

groups in the rates of multivessel disease (52% vs 51%), TIMI flow 0/1 before angioplasty (71% vs 74%), TIMI flow 3 after angioplasty (94% vs 93%), emergency CABG (2% vs 2%) or bleeding complications (2% vs 2%).

Table 3 presents the quantitative coronary angiographic data after the initial procedure and at follow-up. Reference diameters of the BMS and the balloon groups were comparable. The BMS groups had larger luminal diameters and a lower percentage residual diameter stenosis after the initial procedure and at follow-up.

Table 4 presents the rates of reocclusion, restenosis and subacute thrombosis. Reocclusion was less frequent after BMS implantation compared with balloon angioplasty (6.7% vs 10.1%, OR 0.62, 95% CI 0.40 to 0.96, p = 0.03) (fig 2). Also, restenosis was less frequent after BMS implantation compared with balloon angioplasty (23.9% vs 39.3%, OR 0.45, 95% CI 0.34 to 0.59, p<0.001) (fig 3). Six trials reported rates of subacute thrombosis.[7–9 12–14] There was no difference in the rate of subacute thrombosis between the two groups (1.7% in both groups, OR 0.82, 95% CI 0.42 to 1.59, p = 0.55) (fig 4).

Clinical outcome

Table 5 presents clinical outcome. All trials reported all-cause mortality. There was no difference in mortality between the BMS and the balloon groups at the end of follow-up (fig 5). There was no difference in reinfarction rate (fig 6). Rates of non-fatal MI were not given separately in some of the trials, so our reported rates of MI probably include a fraction of fatal cases. For repeat revascularisation, five trials specified the requirement for ischaemic symptoms in order to perform TVR,[5 7 8 10 12] which suggests that in some cases revascularisation has certainly been protocol-driven by the mandatory follow-up angiograms. TVR rates were performed in 12.2% in the BMS group compared with 19.2% in the balloon group, OR 0.50 (95% CI 0.37 to 0.69, p<0.001) (fig 7).

DISCUSSION

The objective of our systematic review was to quantify the treatment effect of the use of BMS compared with balloon angioplasty in primary PCI on angiographic measures of infarct vessel patency, and to relate these angiographic measures to

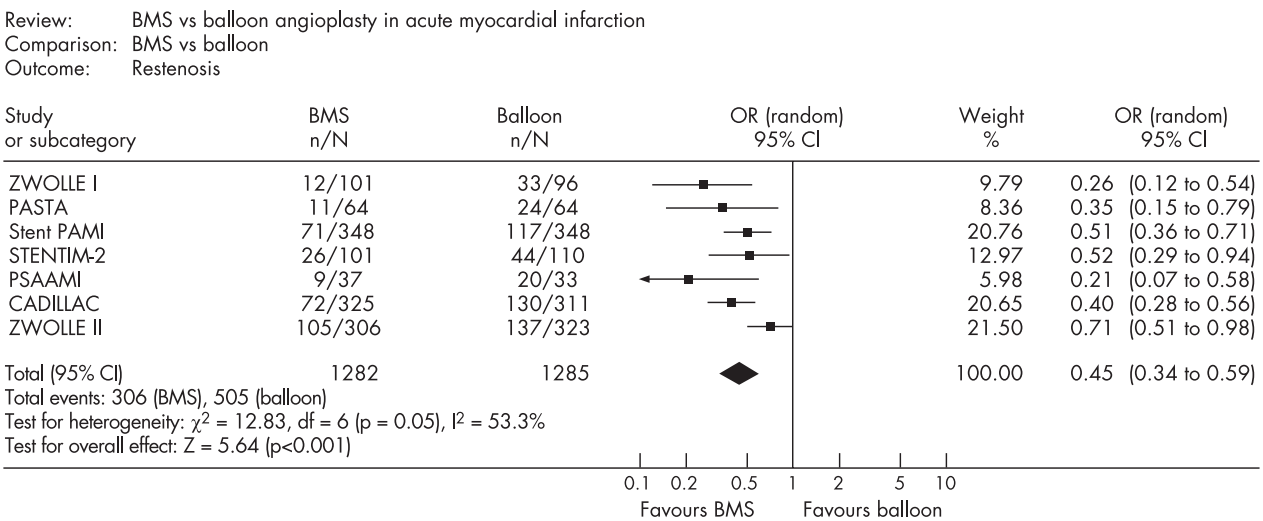

Figure 3 Restenosis. BMS, bare-metal stent.

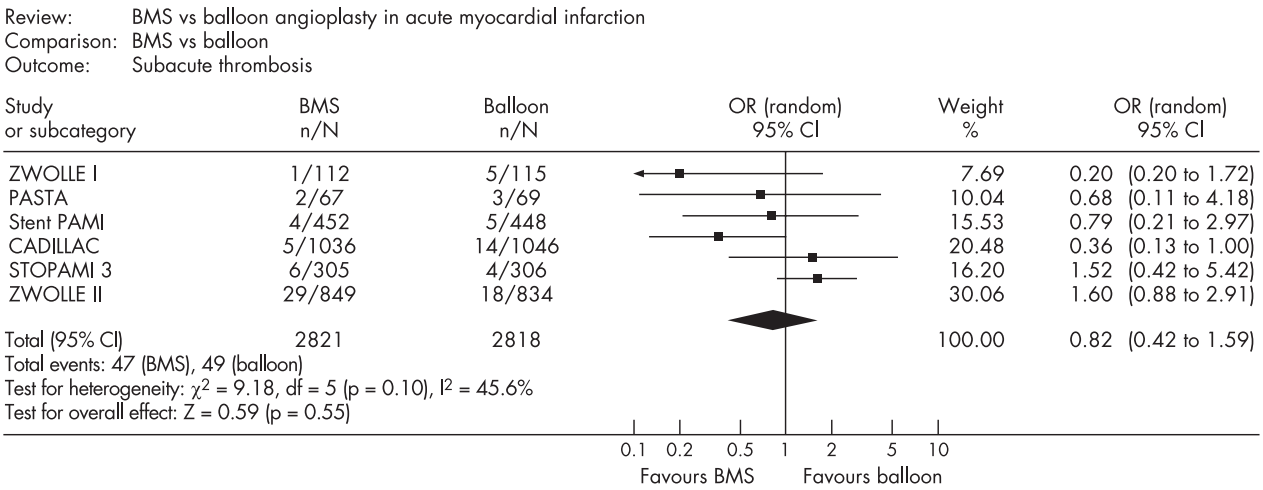

Figure 4 Subacute thrombosis. BMS, bare-metal stent.

clinical outcome in patients with acute MI. We found an important reduction in the rates of reocclusion and restenosis with BMS implantation compared with balloon angioplasty. BMS implantation did not influence the rate of subacute thrombosis. As confirmed by previous studies, our data show that BMS implantation reduces the need for TVR compared with balloon angioplasty. The pooled data showed no clear impact on reduced reocclusion or restenosis rates on mortality or reinfarction rate with BMS implantation compared with balloon angioplasty in patients presenting with acute MI. There were no differences between BMS and balloon angioplasty in the rates of successful reperfusion measured by TIMI flow 3 after the procedure or in the need for emergency CABG. We did not observe a higher rate of bleeding complications with BMS.

The outcome of reocclusion shows a similar pattern as the results of one previously published analysis examining the frequency of reocclusion after balloon angioplasty, BMS placement and thrombolytic therapy in acute MI, which showed lower reocclusion rates after BMS placement than after balloon angioplasty alone (OR 0.28, 95% CI 0.65 to 1.75, $p<0.001$).[33] However, the study was not based on randomised comparisons of the two treatment modalities, which may have been an important source of bias in the analysis.

Although reocclusion has been associated with depressed left ventricular function and a poor outcome, both after thrombolytic treatment[23 24] as well as after PCI,[24–26] the difference in reocclusion rates in our pooled analysis did not seem to translate into a difference between the BMS and the balloon groups in mortality at 1 year of follow-up. One explanation for this finding could be that a reoccluded infarct-related artery and depressed left ventricular function may require a longer follow-up duration than 1 year to become clinically apparent.[1 23–26] Indeed, a mortality benefit of BMS placement seems to be less obvious in trials with a shorter follow-up period. An exception is the Stent PAMI trial in which a higher mortality rate in the BMS group despite a reduced reocclusion rate could be related to lesser number of patients with post-procedural TIMI 3 flow in the BMS group compared with the balloon group. Another possible explanation could be the timing of follow-up angiography at 6 months, which is mainly based on analyses with balloon angioplasty showing that the majority of restenosis occurs within the first 3 months after the procedure.[34] With coronary BMS opposing early elastic recoil of the vascular lumen as well as late vascular remodelling and thereby increasing luminal diameter, the time course of restenosis and reocclusion due to neointimal hyperplasia could be delayed. Hence, some patients in the BMS group may develop restenosis or reocclusion beyond the time of angiographic follow-up as compared with the balloon angioplasty group. This may lead to an underestimation of these rates in the BMS group.

Despite lower overall rates of reocclusion and restenosis with BMS, there were no significant differences between the BMS

Table 5 Clinical data at follow-up

	Randomisation		Mortality		ReMI		TVR	
	BMS	B	BMS	B	BMS	B	BMS	B
TRIAL	n		n (%)		n (%)		n (%)	
FRESCO[5]	75	75	1	0	1	2	5	19
GRAMI[6]*	52	52	2	4	0	4	7	10
ZWOLLE I[7]	112	115	3	4	1	10	15	39
Stent PAMI[8]	452	448	25	15	16	11	47	93
PASTA[9]	67	69	3	6	0	4	12	24
STENTIM-2[10]	101	110	3	2	4	5	17	25
PSAAMI[11]	44	44	4	8	1	4	7	15
CADILLAC[12]	1036	1046	37	36	20	23	76	166
STOPAMI 3[13]	305	306	25	28	7	4	25	32
ZWOLLE II[14]	849	834	60	55	71	57	166	173
Total	3093	3099	163 (5.3)	158 (5.1)	121 (3.9)	124 (4.0)	377 (12.2)	596 (19.2)

BMS, bare-metal stent group; B, balloon group; PAMI, Primary Angioplasty in Myocardial Infraction; ReMI, reinfarction; TVR, target vessel revascularisation.
*Mortality and ReMI at 30 days.

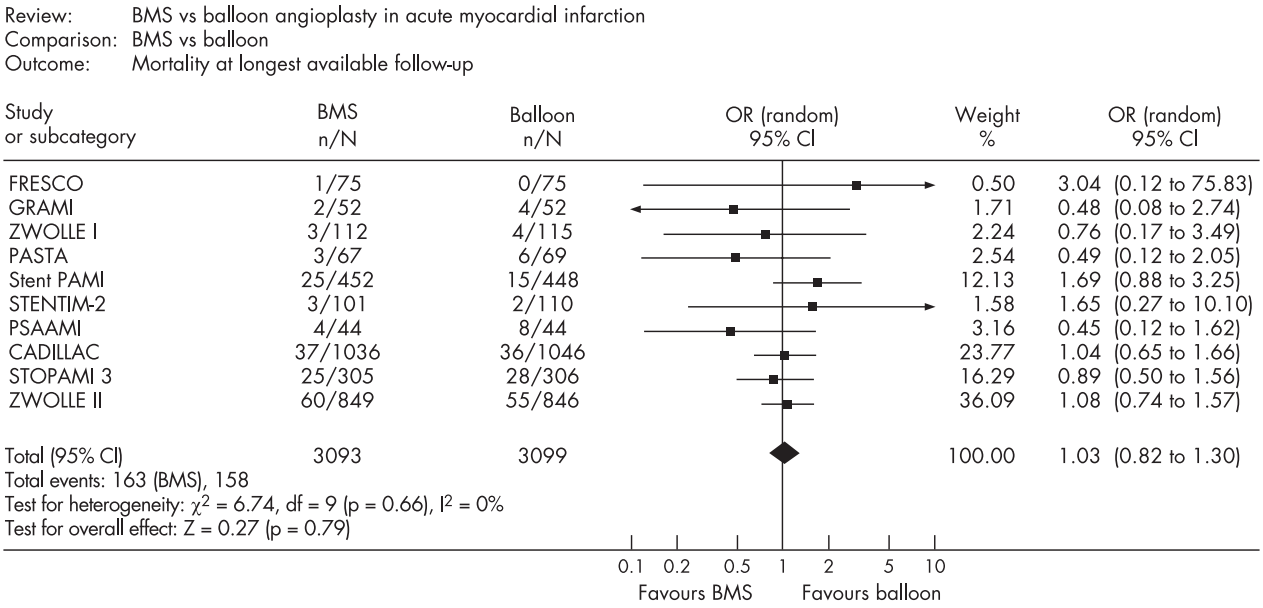

Figure 5 Mortality at longest available follow-up. BMS, bare-metal stent.

and the balloon angioplasty groups in terms of subacute thrombosis. One explanation for this finding is that the rates of subacute thrombosis in the individual trials are low and more data may be needed to show a significant difference between the groups. An alternative explanation is that the pathophysiological mechanisms for restenosis and subacute thrombosis may differ. A beneficial effect of BMS on luminal diameter on the longer term may initially be opposed by the increased risk of thrombus formation before neointimal stabilisation of the stent.

The ZWOLLE II trial,[14] with 1683 of 6192 (27.2%) patients in our analysis, randomised consecutive patients in a single centre. Interestingly, this trial shows no benefits of coronary BMS compared with angioplasty in terms of reocclusion, restenosis and TVR. The study enrolled patients before coronary angiography, thereby decreasing the bias of preselecting patients. However, the study design resulted in high crossover rates, both from balloon to BMS as well as from BMS to balloon. As a consequence, the intention-to-treat analysis and the per-protocol analysis of this trial show different results. This trial shows that coronary BMS can be applied in 85–90% of patients with ST-elevation MI.

There seems to be an association between timing of randomisation with respect to coronary angiography and cross-over rates. The mentioned ZWOLLE II trial[14] was the only trial with randomisation of patients before coronary angiography. A total of 3232 of 6192 (52.2%) patients were enrolled in six trials[6 9–13] with randomisation after coronary angiography, but before initial reperfusion was obtained with wire and balloon. These trials are characterised by a lower crossover rate

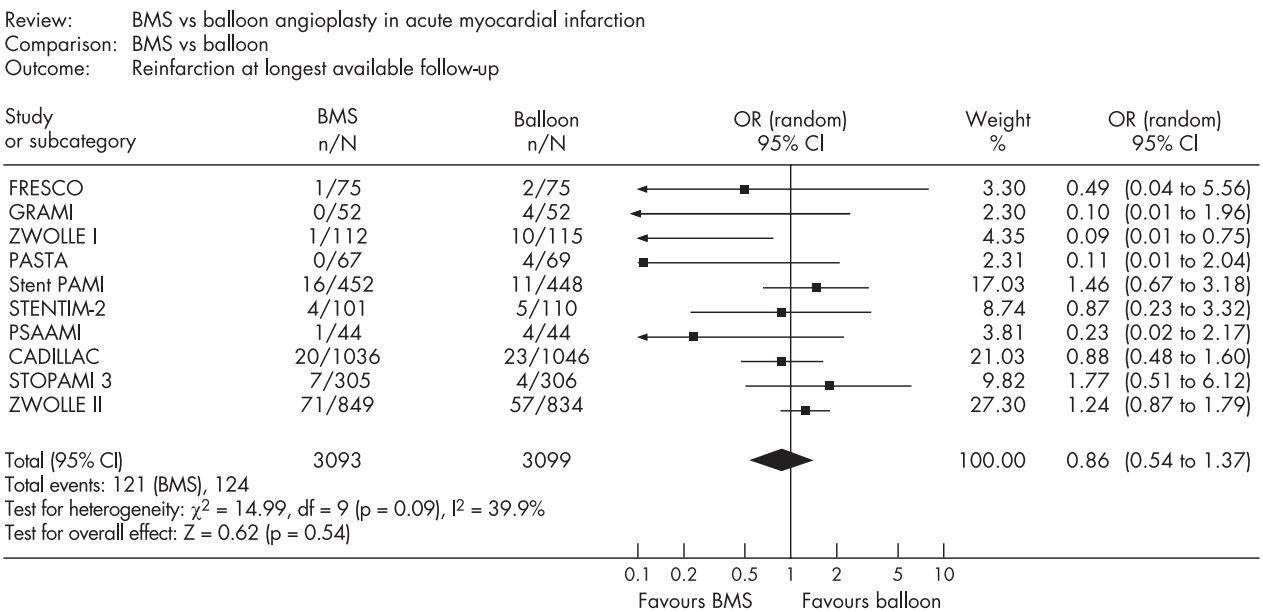

Figure 6 Reinfarction at longest available follow-up. BMS, bare-metal stent.

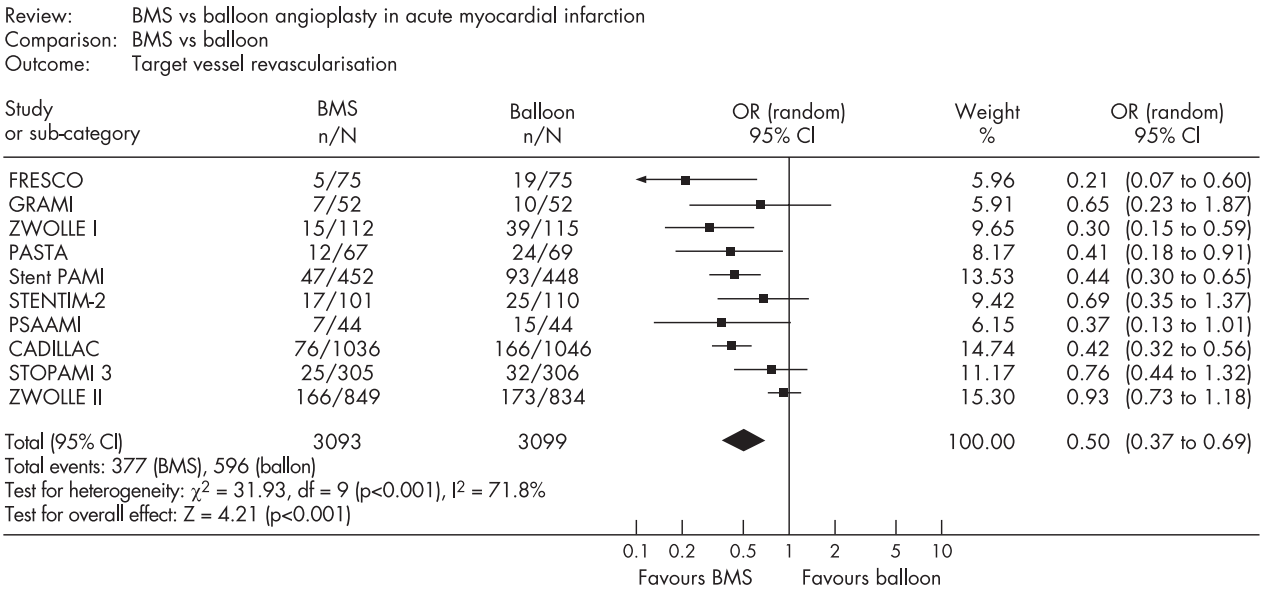

Figure 7 Target vessel revascularisation. BMS, bare-metal stent.

from balloon to BMS implantation than in the ZWOLLE II trial as a result of the used coronary angiographic inclusion and exclusion criteria. Three trials[5 7 8] enrolled patients (1277 of 6192, 20.6%) after coronary angiography and reperfusion with wire and balloon. Cross-over rates in these three trials were low and varied somewhat according to study design.

In primary PCI, as in elective PCI, it has been difficult to show that BMS placement reduces rates of mortality and reinfarction. With the introduction and ongoing investigation of the benefit of drug-eluting stents during PCI, it is unlikely that prospective studies to address the question of mortality and reinfarction after BMS placement compared with balloon angioplasty will be performed. As reocclusion, restenosis and TVR are the major differences in outcome after BMS compared with balloon angioplasty, it can be expected that technical improvements in mechanical reperfusion therapy will further enhance the benefits of stent implantation in terms of these outcome parameters.

LIMITATIONS

We performed our search and selection of trials in accordance with the Quality of Reporting of Meta-Analyses guidelines.[32] Nevertheless, this procedure does not give full protection against the consequences of publication bias. Significant results are more likely to get published than non-significant ones. Some of the other meta-analyses have included data from additional non-published trials of BMS implantation compared with balloon angioplasty. We have chosen not to include the data from these trials as methodology, patient selection, endpoint definitions and the use of core laboratory angiographic analysis are available only in a published, peer-reviewed manuscript. Another limitation of our approach is that we did not have access to the data of individual patients. Subgroup analyses according to specific clinical or angiographic characteristics would certainly provide important additional clinical insights. Moreover, the effect of crossover on the results cannot be determined. Also, the results are not directly applicable to the treatment of small coronary vessels.

Further limitations are the sources of clinical heterogeneity between the trials. Firstly, some of the studies were designed to randomise the patients after successfull balloon angioplasty,[5 7 8] which might have resulted in an underestimation of the true effect of BMS. Furthermore, even though angiographic results are partially standardised by the use of angiographic core laboratories, we cannot exclude unmeasured differences in the outcomes across the studies. Finally, changing trends in the use of concomitant pharmacotherapy and the remarkable progress in stent technology has resulted in pharmacological and technical differences between the early trials and the more recent studies, which may also have influenced the results.

CONCLUSIONS AND CLINICAL IMPLICATIONS

Intracoronary stent implantation has become the principal reperfusion technique after initial recanalisation with wire and balloon in patients with ST-elevation MI. Compared with balloon angioplasty supported by provisional stenting, routine BMS implantation results in an impressive benefit in terms of reocclusion and restenosis. There was no difference in the rate of subacute thrombosis between the two groups. As confirmed by previous studies, there are benefits from BMS compared with balloon angioplasty in terms of TVR. These findings do not seem to translate into a mortality benefit or a lower rate of reinfarction in the pooled data, but a longer follow-up period may be needed to detect a deleterious effect of a reocclusion of the infarct-related vessel. As current practice is mainly based on a beneficial effect of BMS on revascularisation rate as a measure of infarct-related vessel patency, we believe our angiographic findings support BMS placement in acute MI. Moreover, the discrepancy between angiographic and clinical outcome measures has important implications for future studies investigating further technical improvements in mechanical reperfusion therapy, such as the use of drug-eluting stents and devices for distal protection of the infarct-related vessel.

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